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PATENT TRADEMARK OFFICE

Docket No.: 5432/0K116US0

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Andrea CASTELLIN ET AL.

Serial No: 10/035,005

Group Art Unit: 1625

Filed: December 20, 2001

Examiner: Bernard I. DENTZ

Confirmation No: 1065

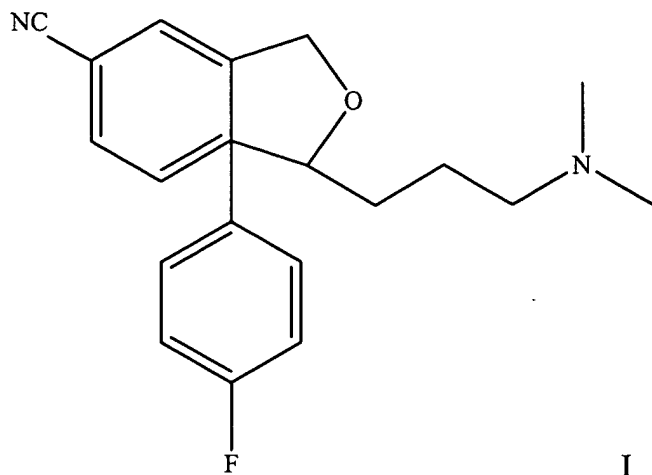
For: PROCESS FOR THE PREPARATION OF PURE CITALOPRAM

Allowed: October 28, 2002

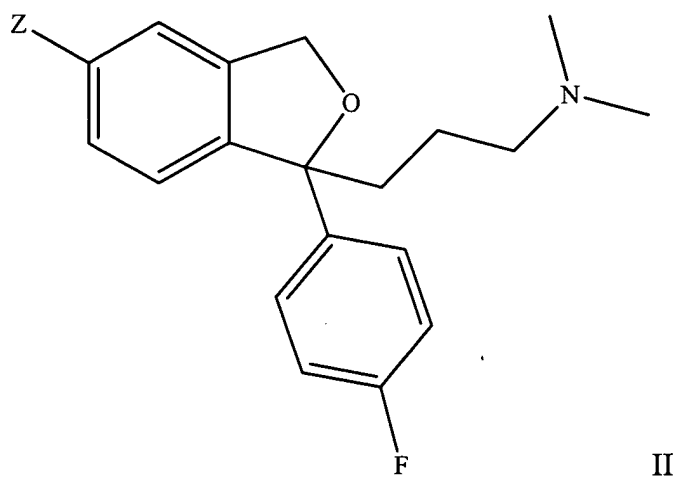
**CLAIMS PENDING AFTER AMENDMENT**  
**ACCOMPANYING REQUEST FOR CONTINUED EXAMINATION**

Assistant Commissioner for Patents  
Washington DC 20231

1. A process for the preparation of citalopram of formula I



in which a compound of formula II



wherein Z is iodo, bromo, chloro or  $\text{CF}_3\text{-(CF}_2\text{)}_n\text{-SO}_2\text{-O-}$  ; and

n is 0, 1, 2, 3, 4, 5, 6, 7 or 8;

is subjected to a cyanide exchange reaction in which the group Z is exchanged with cyanide by reaction with a cyanide source;

the resultant crude citalopram product is optionally subjected to some initial purification

and the crude citalopram base is subsequently subjected to a film distillation process;

the resulting citalopram product is then optionally further purified and worked up and isolated as the base or a pharmaceutically acceptable salt thereof.

2. The process of claim 1, wherein the film distillation process is short path or thin film layer distillation.

3. The process of claim 2, wherein the film distillation process is thin film layer distillation.

4. The process of claim 1, wherein the crude citalopram base is dissolved in an appropriate solvent before it is subjected to film distillation.

5. The process of claim 1, wherein the distillation temperature is 200-330°C and the pressure is 0.1-2.0 mmHg.

6. The process of claim 5, wherein the distillation temperature is 240-270°C and the pressure is 0.6 - 0.8 mmHg.

7. The process of claim 1 wherein Z is bromo and the cyanide exchange reaction is carried out by reaction with cuprous cyanide in a suitable solvent.

8. The process of claim 1 wherein Z is iodo, bromo, chloro or  $\text{CF}_3\text{-(CF}_2)_n\text{-SO}_2\text{-O-}$ , n is 0, 1, 2, 3, 4, 5, 6, 7 or 8, and the cyanide exchange reaction is carried out by reaction with a cyanide source in the presence of a palladium catalyst and a catalytic amount of  $\text{Cu}^+$  or  $\text{Zn}^{2+}$ .

9. The process of claim 1 wherein Z is iodo, bromo, chloro or  $\text{CF}_3\text{-(CF}_2)_n\text{-SO}_2\text{-O-}$ , n is 0, 1, 2, 3, 4, 5, 6, 7 or 8, and the cyanide exchange reaction is carried out with  $\text{Zn(CN)}_2$  in the presence of a palladium catalyst.

10. The process of claim 8, wherein Z is bromo.

11. The process of claim 1, wherein Z is chloro or bromo and the cyanide exchange reaction is carried out with a cyanide source in the presence of a nickel catalyst.

12. The process of claim 8, wherein Z is chloro.

13. The process of claim 4 wherein the solvent is sulfolane.

14. The process of claim 11 which occurs in the presence of a catalytic amount of  $\text{Cu}^+$  or  $\text{Zn}^{2+}$ .

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